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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/665,728	09/20/2000	Lawrence W. Stanton	SCIOS.013A	8743

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EXAMINER
O HARA, EILEEN B

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 10/22/2002 14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/665,728	STANTON ET AL.	
	Examiner	Art Unit	
	Eileen B. O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 30-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 30-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-8 and 30-33 are pending in the instant application. Claims 1-6 and 8 have been amended and claims 30-33 have been added as requested by Applicant in Paper Number 13, filed July 26, 2002.

All claims are currently under examination.

Drawings

2. The objection to the drawings is withdrawn in view of Applicants' submission of new Figure 2.

Specification

3. Pages 45-56 of the specification are missing. It is not known if they were originally submitted with the application and were misplaced at the USPTO, or if they were not with the application as originally filed. It is requested that Applicant submit proof that the pages were with the application as filed, such as a post card filing receipt.

Withdrawn Rejections

4.1 The rejection of claims under 112 § 1 for new matter is withdrawn in view of Applicants' amendment.

4.2 The rejection of claims under 112 § 2 is withdrawn in view of Applicants' amendment.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. The rejection of claims 1-8 is maintained and new claims 30-33 are rejected under 35 U.S.C. 101 because, the claimed invention is not supported by either a specific, credible and substantial asserted utility or a well established utility, for reasons cited in the previous Office Action, Paper No. 12, at pages 3-5.

Applicants traverse the rejection and assert that a prima facie case of lack of utility has not been established. Applicants submit that the Guidelines state that "the utility of a claimed DNA does not necessarily depend on the function of the encoded gene product.", and that the claimed polynucleotides serve as useful probes or markers for specific diseases, independent of the function of the encoded polypeptides. Applicants also submit that agents that diagnose disease during or after its onset or that monitor disease progression have substantial utility, and that that the disclosed in vivo myocardial infarction model supports such a utility for the claimed polynucleotides. Applicants assert that the claimed polynucleotides are differentially expressed in an in vivo model of myocardial infarction, and that the polynucleotides of the invention are useful as probes and primers for nucleic acid amplification procedures for the diagnosis of myocardial infarction, and that this utility is specific and substantial because it has a "real world" application in the diagnosis of a particular disease state. In addition to the invention's utility in myocardial infarction diagnosis, Applicants teach that P00210_D09 mRNA demonstrated

significantly decreased expression in response to growth-factor induced cardiac hypertrophy, thus supporting a role for this sequence as "a downstream mediator of known factors that induce cardiac hypertrophy", and assert that these data support a specific and substantial utility for the claimed polynucleotides and their encoded polypeptides as drug targets for the treatment of cardiac hypertrophy. Applicants supply the references of Heller et al. and Schena, that describe differential gene expression analysis using microarray technology as useful in various applications, including human disease diagnostics, and that the approximately two fold increase in expression level of P00210_D09 mRNA would be a significant and reliable diagnostic marker, given that the sensitivity of microarray analysis. Applicants further note that the Utility Examination Training Materials state that "any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a specific utility."

Applicants' arguments have been fully considered but are not deemed persuasive. While it is true that knowledge of the function of an encoded polypeptide is not necessary for a nucleic acid molecule to have utility, the nucleic acid molecule must have at least one specific and substantial "real world" utility. Applicants assert that the utility of the P00210_D09 polynucleotide sequences are due to their use as a diagnostic of myocardial infarction during or after onset of the disease, or use to monitor disease progression. Microarray analysis can be a useful tool in disease diagnostics for some applications, however, it is not a practical "real world" use in the instant situation. In order to determine if there is a change in expression of P00210_D09 during a possible myocardial infarction or to monitor disease progression, heart tissue would have to be removed from the patient in order to extract mRNA for the analysis. As

a practical matter, surgeons would not take tissue samples from a patient's heart several times or even once to use for diagnosis or to monitor disease progression. If samples could be removed from a patient easily and non-invasively, such as from blood or other fluid samples, and subsequently analyzed, such a method of diagnosis may possibly have some utility. However, the necessity of extracting heart tissue from patients in order to perform the assay makes it prohibitive. At this time, the only use for the polynucleotides and encoded polypeptide is to further study the gene and encoded protein to determine its potential biological significance. Additionally, the fact that P00210_D09 expression increases during myocardial infarction but decreases in the *in vitro* model of cardiac hypertrophy indicates that much more research is needed in order to determine the role of P00210_D09 in cardiac conditions and diseases. For these reasons and those discussed in the previous Office Actions, the rejection under 35 U.S.C. 101 is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6.1 Claims 1-8 are rejected and new claims 30-33 are rejected under 35 U.S.C. 112, first paragraph, for reasons cited in the previous Office Actions, Paper No. 12, at pages 5-6. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Even if the specification were enabling, enablement would not be found to be commensurate in scope with the claims for

reasons cited in the Previous Action. Additionally, the claims are not enabled for an in vitro cardiac disease model having the polynucleotide of SEQ ID NO: 2 differentially expressed by at least about 1.8 fold. The only in vitro cardiac disease model disclosed in the specification is that of cardiac hypertrophy, wherein rat cardiac myocytes were treated with various growth factors and cytokines known to induce cardiac hypertrophy. After treatment, expression of P00210_D09 was decreased, not increased, as in the MI model. From these conflicting data it is not predictable if the levels of P00210_D09 would increase or decrease. For these reasons the rejection under 35 U.S.C. 112, first paragraph is maintained.

6.2 Claims 1 and 5-8 remain rejected, and new claims 30, 32 and 33 are also rejected under the written description requirement of 35 U.S.C. 112, first paragraph, for reasons cited in the previous Office Actions, Paper No. 12, at pages 6-8.

Applicants traverse the rejection and submit that the claims as amended are fully supported by the single representative polynucleotide species of SEQ ID NO: 2, and that the USPTO's Written Description Guidelines states that an applicant may satisfy the written description requirement "by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention." Applicants assert that the claims recite polynucleotides with a common feature, that is, ability to detect, by microarray analysis, a polynucleotide that is differentially expressed by at least about 1.8-fold in an in vivo or in vitro cardiac disease model, and although Applicants disclose only a single representative species (SEQ ID NO: 2) having this feature, this species is adequate to demonstrate that Applicants were in possession of a genus of polynucleotides having this particular feature.

Applicants' arguments have been fully considered but are not deemed persuasive. The instant application presents results from one type of in vivo experiment, the myocardial infarction model, in which expression of P00210_D09 was increased approximately 2 fold by microarray analysis. The disclosure also presents results from one type of in vitro experiment, the cardiac hypertrophy model, wherein rat cardiac myocytes were treated with various growth factors and cytokines known to induce cardiac hypertrophy, and in which after treatment, expression of P00210_D09 was decreased, not increased, as in the MI model. Results from two different experiments, in which differential expression of P00210_D09 is either increased or decreased, does not provide adequate support for differential expression of P00210_D09 in any cardiac disease model, and especially in light of the fact that the differential expression from the two types of models produce different results. Therefore, the rejection under 35 U.S.C. 112, first paragraph is maintained.

It is believed that all pertinent arguments have been answered.

Conclusion

6. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examine

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
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